The opinion in support of the decision being entered today was **not** written for publication and is **not** binding precedent of the Board.

#36

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LIU ET AL

Appeal No. 2005-0974
Application 09/229,226

On BRIEF

Before FRANKFORT, PATE, and HORNER, *Administrative Patent Judges*.

PATE, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal from the final rejection of claims 1-33. These are the only claims in the application.

The claimed invention is directed to a method and apparatus for altering cell viability for the transport of chemicals or biological agents into or through internal organs, internal tissues, or vessels in humans or other animals. The method uses ultrasonic energy. A feedback mechanism by which the application of ultrasonic energy is controlled is also claimed. Reference is made to the appealed claims appended to appellants' brief for further details of appellants' claimed invention.

THE REFERENCES

The following references relied upon by the examiner as evidence of anticipation and obviousness are:

Eppstein et al.	5,445,611	August 29, 1995
Bommannan et al.	5,636,632	June 10, 1997
Klopotek	6,113,559	September 5, 2000

Tachibana et al., "Albumin Microbubble Echo-Contrast Material as an Enhancer for Ultrasound Accelerated Thrombolysis," *Circulation*, Vol. 92 No. 5 September 1, 1995

THE REJECTIONS

Claims 1-25 and 27-33 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

Claims 1, 2, 10, 11, 14, 15, 17, 19, 21, and 23-28 stand rejected under 35 U.S.C. § 102(e) as anticipated by Klopotek.

Claims 27, 28, and 30 stand rejected under 35 U.S.C. § 102(b) as anticipated by Eppstein.

Claim 22 stands rejected under 35 U.S.C. § 103 as unpatentable over Klopotek.

Claims 1-5, 8-18, 23-26, and 29 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Eppstein in view of Klopotek.

Claims 1-3, 5,7, 14, 15, 18, 23, and 25-27 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Tachibana in view of Klopotek.

Claims 6 stands rejected under 35 U.S.C. § 103 as unpatentable over Eppstein in view of Klopotek and Bommannan.

For the details of these rejections, reference is made to the examiner's answer. For a further understanding of appellants' arguments with respect to these rejections, reference is made to the brief and reply brief.

OPINION

We have carefully reviewed the rejections on appeal in light of the arguments of the appellants and the examiner. As a result of this review, we affirm all standing rejections of claims 1-19 and 21-30 made under §§ 102 and 103 of the statute. These are all the prior art rejections on appeal. We also affirm the rejection of claims 1-25 under 35 U.S.C. § 112, second paragraph. However, we reverse the standing 112, second paragraph rejection of claims 27-33. Our reasons follow.

Turning first to the rejection under § 112, second paragraph, we sustain the rejection of claim 1 and the claims dependent thereon with respect to the administering step of claim 1. We agree with the examiner that it is unclear whether this is an additional administering step from the administering step of independent claim 27 or is a second recitation of the administering step of claim 27. In our view there is not enough information to make an informed decision in this regard, and one

of ordinary skill could not determine the metes and bounds of the claimed subject matter. We regard claim 27 as clear on its face in this regard, however, since it includes only the single administering step. Consequently, we affirm the rejection under the second paragraph of § 112 of claims 1-25. We reverse the rejection to the extent that it involves claim 27-30.[1]

With respect to the standing 112, second paragraph rejection of claims 31-33, we are of the view that the first site recited in claim 27 is not in conflict with the recitation that the transducer is placed inside the body, in a blood vessel or within an incision. The first site could be at any one of those locations. The second paragraph rejection of claims 31-33 is reversed.

Turning to the rejections under sections 102 and 103, the following are our findings of fact with respect to Klopotek. Klopotek shows a method for treating underlying skin tissue to decrease visible wrinkles or rhytides. Klopotek shows an ultrasonic transducer 22, focusing element 24, waveguide 26, and an acoustic coupling medium which could be a hydrogel, 28. The ultrasonic energy passes through a first skin layer or tissue, the

[1] As a further matter, we note the expression ''at a distant second distant site'' in claim 27. We have construed this as - a site distant from said first site -. This ungrammatical expression should be corrected in any further prosecution.

epidermis 14, and is focused in a second tissue layer the dermis at 16 in Figure 1. Klopotek discloses five feedback systems that can be used to control the administration of the ultrasonic energy. See col. 5, line 30 to col. 6, line 55. The theory of operation is that the ultrasonic energy stimulates or irritates the dermis layer of the skin without significant or detrimental irritation of the epidermis layer. Col. 3, lines 40-41. That is, the layer of tissue, the epidermis, next to the transducer is not harmed by the ultrasound while a second layer of tissue, the dermis, remote or distant from the site of application of the transducer to the first tissue layer is treated by the ultrasound. The ultrasound causes activation of fibroblast cells in the dermis.

Col. 1, lines 64-65.

Appellants argue (Brief, page 10), with respect to the Klopotek rejection under section 102, that layers of skin are not different tissues. Brief page 10, lines 7, 8. Appellants refer us to the figures of Klopotek, wherein it is clearly shown that two layers of tissue are involved in the treatment. Absent a definition of "tissue" in appellants' specification, we must give the claim terms their broadest reasonable construction. Appellants have not pointed out a more restrictive definition found in the specification, in their arguments to the examiner, or in the

brief. Further, in the reply brief, appellants argue that the dermis, being part of the skin, cannot be considered an internal organ or internal tissue. We do not need to reach the issue of whether the dermis is an internal organ, inasmuch as we believe that the dermis certainly qualifies as internal tissue. We regard the claim term "tissue" as extremely broad, as it is commonly held to denote an aggregation of similar cells. Since the layer of similar cells called the dermis is not on the external surface of the body, the dermis satisfies the preambular requirement of an internal tissue.

Although we noted above that the specification of appellants does not contain a definition of the term "tissue", we find that the disclosure at page 9, lines 30 and 31 reads as follows: "Representative barriers include mammalian and non-mammalian tissues, including skin, tumor...." Thus it is clear that appellants include skin as a kind of tissue.

Finally, our common understanding of the claim term "tissue" and its relation to the layers of the skin is buttressed by the disclosure of Klopotek:

> Human skin is basically composed of three layers. The outer, or visible layer is the stratum corneum. The stratum corneum is essentially a thin layer of dead skin cells that serves, among other things, as a protective layer. Below the stratum corneum is the epidermis layer. *The epidermis layer is a cellular structure that forms the outermost living tissue of the skin.* Below the

> epidermis layer is the dermis layer that *contains a variety of tissues* such as sweat glands, nerves cells, hair follicles, living skin cells, and *connective tissue. The connective tissue* gives the dermis layer body, shape, and support. Since the epidermis layer lies on top of the dermis layer, the shape, smoothness, and appearance of the epidermis layer is in part determined by the shape of the dermis layer (and largely the connective tissue). Thus, variations in the shape of the *connective tissue* tend to appear as variations in the epidermis layer Col. 1, ll. 13-28 (emphasis supplied).

In the reply brief, appellants take a different tack. Instead of arguing that layers of skin are not different tissues, appellants argue that the dermis is not an *internal* organ or an *internal* tissue. Reply Brief, page 4, lines 7, 8. Here again, appellants argue that the skin is a single tissue. As we have seen from the description quoted from the Klopotek patent, above, the skin is composed of multiple layers of tissues with both of the two inner layers - the epidermis and the dermis - qualifying as internal tissues. In fact, Klopotek clearly discloses that the dermis is composed of multiple tissue types. The claim terms "internal" and "tissue" are very broad, and when we give this claim the broadest reasonable interpretation, appellants' argument in the reply brief is not credited.

Finally, we note appellants' claim 11 wherein tissue is specified as skin. The presence of claim 11 undercuts appellants' argument regarding skin as not a tissue or not an internal tissue.

Simply put, appellants' arguments respecting the § 102 rejection are not credited. It is our finding that Klopotek anticipates claims 1, 2, 10, 11, 14, 15, 17, 19, 21 and 23-28. These claims have not been separately argued and fall together. For independent claim 26, note Figure 6 of Klopotek that discloses a "means for treating...", comprising a transducer 22, a "means for measuring...", sensors 114, 120, 118 used with 116, 112, or 122, and a means for using feedback "to modify...", the controller 102.

With respect to claim 22, rejected under Klopotek alone on obviousness grounds, as far as we can determine, appellants have not challenged the examiner's legal conclusion that the means to analyze the energy measurements in the ultrasound measuring feedback system are an obvious design choice to those of ordinary skill in the ultrasound treatment arts. Since this rejection has not been challenged, we summarily affirm the obviousness rejection of claim 22.

The following are our findings of fact with respect to the Eppstein patent. Eppstein discloses the administration of ultrasonic energy to the skin to alter permeability and thus aid transport of therapeutic or analytic substances. Permeability is one of the goals mentioned in appellants' claim preambles. Appellants admit that Eppstein teaches the application of ultrasound to the skin or mucosa to alter transport through the

skin. Brief, page 10, ll. 14-5. Here again, appellants argue that the inner tissues in the skin, particularly the dermis, are not internal tissues. As explained above, giving the claims their broadest reasonable interpretation, we are of the view that the tissues of the dermis are internal tissues. The rejection of claims 27, 28 and 30 is affirmed.

We further agree with the examiner that the subject matter of claims 1-5, 8-18, 23-26 and 29 is unpatentable over the combined teachings of Eppstein and Klopotek. Eppstein teaches the application of ultrasonic energy to the body to alter permeability and thus aid transport of therapeutic or analytical substances. Klopotek teaches the use of a feedback system to modify the continued application of ultrasound. In our view, it would have been obvious to utilize a feedback system in the method of Eppstein in order to provide for the advantageous effects of ultrasound while minimizing the deleterious effects of ultrasound administration.2

The Tachibana reference is directed to fibrinolytic dissolution of blood clots by the application of albumin containing microbubbles in the presence of ultrasound energy. While the experiments performed were *in vitro*, they are suggestive

2 We note the final two paragraphs of appellants' brief contain a list of claims with a statement of what the claim recites. This cannot be considered an argument for separate patentability.

of using ultrasound, particularly at 170 kHZ. We note that some of appellants' experiments were performed *in vitro.* Tachibana also states that undue heating or chemical reactions should be avoided to prevent damage to vessels and surrounding *tissues.* Thus in our view, it would have been obvious to use ultrasonic energy to alter cells *in vivo* and to use one of the feedback mechanisms disclosed in Klopotek to prevent undue heating or damage to the surrounding tissues and blood vessels as suggested by Tachibana. Accordingly, we affirm the rejection of claims 1-3, 5, 7, 14, 15, 18, 23 and 25-27 as unpatentable over the collective teachings of Tachibana and Klopotek.

Bommannan discloses applied material delivery by enhancing permeability of tissue in topical, transdermal or transmucosal administration by the use of ultrasound. Bommannan discloses that skin is a relatively impermeable barrier composed of different tissue layers having different resistances to penetration by various molecules desired to be delivered. See col. 1, lines 30-52. Although appellants state that Bommannan makes no reference to applying a transducer to the skin and looking for an effect in an internal tissue or organ, Bommannan clearly does contemplate such effects. For example, Bommannan defines transdermal or percutaneous as passage of a material into and through the skin to achieve effective therapeutic blood levels or deep tissue levels.

Col. 5, lines 16 and 17. Appellants are apparently of the view that Bommannan is only concerned with topical administration, which Bommannan defines as penetrating into the skin, but not through it, i.e., topical administration does not involve actual passage of a drug into the bloodstream. Col. 5, lines 32-35. However, Bommannan is replete with discussions of transdermal or transmucosal administration as opposed to mere topical administration. Appellants' arguments respecting Bommannan are simply not credible.

We further note that Bommannan contemplates using ultrasonic energy as a non-invasive diagnostic technique wherein a sampling chamber is used in conjunction with the ultrasonic energy to facilitate sampling of physiological material from beneath the surface of the skin. See col. 4, lines 54-59. With this teaching in mind, it is our legal conclusion that the subject matter of claim 6 would have been obvious from the collective teachings of Bommannan, Klopotek and Eppstein for the reasons advanced by the examiner. Accordingly, we affirm the standing § 103 rejection of claim 6.

SUMMARY

We have affirmed all standing rejections of claims 1-19, and 21-30 made under § 102 and 103 of the statute. These are all the prior art rejections on appeal. We have also affirmed the

rejection of claims 1-25 under § 112, second paragraph. We reverse the standing 112, second paragraph rejection of claims 27-33.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

CHARLES E. FRANKFORT)
Administrative Patent Judge)
)
)
) BOARD OF PATENT
WILLIAM F. PATE III)
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
LINDA E. HORNER)
Administrative Patent Judge)

Appeal No. 2005-0974
Application No. 09/229,226

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361